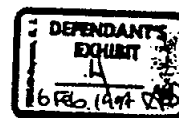


7

joint Peter File
Zantac synth Roubil Syn
These yellowing pages
from my own file
now I was the
nearest to being an
inventor
Dae
30/1187

GLAXO WELLCOME INC. AND GLAXO GROUP LIMITED v. PHARMABODY CORPORATION
CIVIL ACTION NO. AND 16-455 HIGHLY CONFIDENTIAL UNDER PROTECTIVE ORDER



Y010984



MM, KW, PK, JV, DL, D. Mendel, A. Santoro, M. Zuckerman
Zantac Syrup Options as 1 see item 16/8/85

UK ① Launch - a 6° storage restriction
 Adv. - Earliest launch

Disadv. less convenient to use
 May get ridiculous undeserved reputation for instability

② Check ETOH is OK - can a lower %?
 - medically
 - stability ← 2-3 weeks

Check whether ETOH + protein or not in form?
 ③ If ETOH OK put up stability studies

Say mid Sept
 3m data off analysis - early Jan
 Target ISC tight for Jan O.K. for Feb '86

USA either
 ① Put in NDA with 6° storage restriction
 ② Advise Glaxo - that formula is O.K. for cream pack

OR Put ETOH formulation on stability (would need more bottles/cup exp PET).

done.
 - Chlorhexidine ?? Try to kill it. ICI oral toxicity.
 - Phenoxethanol it is designed to kill P. cep. unknown pH7.
 (look 80°/10min)

Look at 2 levels. Taste? Solubility? Add to
 Benzalkonium / Taste | Micro | Analytical | Stringer Toxicology
 ① ② ③ ④ ⑤

Summary Propyl + Butyl Alcohol =
 5% Ethanol paper by ASD 3% + 1% (in 3-4 weeks)
 Phenoxethanol at two levels 0.5 1.0 u. when used, phed make solution 0.1%?
 B.K. how PET get Pack?

swac group4/10/85
26-10-85Points

1. Formulation proposed for marketing is effective against P. capacia when propyl and butyl are at least spec lower limit 70% provided 5% EtOH is included
 2. EtOH 3% and EtOH 1% only prevent proliferation - do not kill
 3. Need to check that EtOH 5% does not have significant effect on rate of hydrolysis of paracetamol or tranexamsylate (check 65° due 9/10/85). If it does, we would have to avoid EtOH and go for phenylethanol (see 6).
 4. Need confirmation that EtOH 5% is medically and commercially acceptable.
 5. Need challenge at 4%, 4.5% EtOH with a check quat: 80-110%.
 6. The effect of ethanol concentration 5, 3, 1% is also seen with the preliminary (nethyl, propyl and butylhydroxybenzoate) formulation and with ethyl, propyl and butylhydroxybenzoate formulation
 7. Phenylethanol at acceptable concⁿ for taste, 0.25% w/v, is as effective as 5% EtOH when added to form proposed for marketing.
= chemically compatible = suitable
without preservative for oral use but mainly req^d this is because of taste
 8. Phenol at acceptable concⁿ for taste 0.005% is ineffective
 9. Returning to the nethyl formulation but increasing the concⁿ to new satⁿ at 4% gives no improvement
- Do 7.5% rates / taste / clarity